

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference GWS/MM/22204	FOR FURTHER ACTION		see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
International application No. PCT/GB 00/ 00873	International filing date (day/month/year) 10/03/2000	(Earliest) Priority Date (day/month/year) 10/03/1999	
Applicant ASM SCIENTIFIC, INC. et al.			

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :
- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of Invention is lacking** (see Box II).

4. With regard to the title,

- ☒ the text is approved as submitted by the applicant.
- ☐ the text has been established by this Authority to read as follows:

5. With regard to the abstract,

- ☒ the text is approved as submitted by the applicant.
- ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

- ☒ as suggested by the applicant.
- ☐ because the applicant failed to suggest a figure.
- ☐ because this figure better characterizes the invention.

3
☐ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

T/GB 00/00873

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, MEDLINE, BIOSIS, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 05315 A (DENSAM DANIEL HENRY ;MEDICAL BIOSYSTEMS LTD (GB)) 4 February 1999 (1999-02-04) the whole document	1-23
A	WO 96 31622 A (ISIS INNOVATION ;SOUTHERN EDWIN MELLOR (GB); PRITCHARD CLARE ELIZA) 10 October 1996 (1996-10-10) the whole document	
A	WO 90 13666 A (AMERSHAM INT PLC) 15 November 1990 (1990-11-15) the whole document	
A	WO 93 21340 A (MEDICAL RES COUNCIL ;BRENNER SYDNEY (GB); ROSENTHAL ANDRE (GB)) 28 October 1993 (1993-10-28) the whole document	
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Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

18 August 2000

Date of mailing of the international search report

28/08/2000

Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

International Application No

T/GB 00/00873

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	GB 2 102 005 A (MTA KOEZPONTI KEMIAI KUTATO IN) 26 January 1983 (1983-01-26) the whole document ---	
A	DATABASE WPI Derwent Publications Ltd., London, GB; AN 1998-437489 XP002145019 & WO 98 33939 A (HITACHI LTD ;ANAZAWA TAKASHI (JP); KAMBARA HIDEKI (JP); OKANO KAZU), 6 August 1998 (1998-08-06) abstract ---	
A	WO 91 06678 A (STANFORD RES INST INT ;TSIEN ROGER Y (US)) 16 May 1991 (1991-05-16) the whole document ---	
A	WO 94 21822 A (KOESTER HUBERT) 29 September 1994 (1994-09-29) the whole document ---	
E	WO 00 36152 A (WILLIAMS JOHN G K ;LI COR INC (US)) 22 June 2000 (2000-06-22) the whole document -----	1-23

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No



T/GB 00/00873

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 9905315	A	04-02-1999	AU 8455998 A EP 1017848 A		16-02-1999 12-07-2000
WO 9631622	A	10-10-1996	EP 0820524 A JP 11503019 T		28-01-1998 23-03-1999
WO 9013666	A	15-11-1990	CA 2045505 A EP 0471732 A JP 4505251 T		12-11-1990 26-02-1992 17-09-1992
WO 9321340	A	28-10-1993	AT 159766 T AU 4020893 A CA 2133956 A DE 69314951 D DE 69314951 T EP 0640146 A ES 2110604 T JP 7507681 T US 6087095 A		15-11-1997 18-11-1993 28-10-1993 04-12-1997 19-03-1998 01-03-1995 16-02-1998 31-08-1995 11-07-2000
GB 2102005	A	26-01-1983	NONE		
WO 9833939	A	06-08-1998	NONE		
WO 9106678	A	16-05-1991	CA 2044616 A EP 0450060 A		27-04-1991 09-10-1991
WO 9421822	A	29-09-1994	AU 687801 B AU 6411694 A CA 2158642 A EP 0689610 A JP 8507926 T US 5622824 A US 5872003 A US 5851765 A US 6074823 A		05-03-1998 11-10-1994 29-09-1994 03-01-1996 27-08-1996 22-04-1997 16-02-1999 22-12-1998 13-06-2000
WO 0036152	A	22-06-2000	WO 0036151 A		22-06-2000

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference GWS/MM/22204		FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/GB00/00873	International filing date (day/month/year) 10/03/2000	Priority date (day/month/year) 10/03/1999	
International Patent Classification (IPC) or national classification and IPC C12Q1/68			
Applicant ASM SCIENTIFIC, INC. et al.			
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 7 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>			
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none">I <input checked="" type="checkbox"/> Basis of the reportII <input type="checkbox"/> PriorityIII <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicabilityIV <input type="checkbox"/> Lack of unity of inventionV <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statementVI <input checked="" type="checkbox"/> Certain documents citedVII <input checked="" type="checkbox"/> Certain defects in the international applicationVIII <input checked="" type="checkbox"/> Certain observations on the international application			
Date of submission of the demand 22/09/2000		Date of completion of this report 05.06.2001	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized officer Tilkorn, A-C Telephone No. +49 89 2399 8688 	

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/00873

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-33 as originally filed

Claims, No.:

1-23 as originally filed

Drawings, sheets:

1/8-8/8 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/00873

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-13,19-23
	No:	Claims	14-18

Inventive step (IS)	Yes:	Claims	-
	No:	Claims	1-23

Industrial applicability (IA)	Yes:	Claims	1-23
	No:	Claims	-

2. Citations and explanations
see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB00/00873

Re Item V

The following documents are referred to in this communication:

D1: WO 99 05315 A 4 February 1999
D2: WO 90 13666 A
D3: WO 93 21340 A
D4: WO 00 36152 A 22 June 2000

1 Novelty (Art 33(2) PCT):

- 1.1 The subject-matter of **claim 14** is anticipated by D1, which discloses a system for nucleic acid sequence analysis which embraces a polymerase enzyme immobilized on a solid support, a nucleic acid sample and a primer (abstract; claim 1, p 5 l 33- p 6 l 2, p 7 l 4-13; p 11 l 22 ff). D1 is also prejudicial to the novelty of **claims 15-18** (D1: p 6 l 15-29).
- 1.2 **Claim 19** is novel, because none of the available documents discloses an array of immobilized polymerase systems. Dependent **claims 20-23** are novel accordingly.
- 1.3 **Claim 1** is novel, because none of the available documents describes a method for nucleic base sequencing involving four different nucleotides each nucleotide being differentially-labelled with a detachable labelling group. Dependent **claims 2-13** are novel accordingly.

2 Inventive Step (Art 33(3) PCT):

- 2.1 **Claim 1** does not appear to satisfy Art 33(3) PCT for the following reasons:
D1, which is considered to represent the closest prior art, describes sequencing methods (D1: p 2 l 25- p 3 l 24) which differ from the method according to claim 1 only in that the different nucleotides used in D1 do not contain a detachable labelling group. In the method of D1 the distinction between the different nucleotide bases is achieved by the different kinetic behaviour for the incorporation of the nucleotides into the nascent oligonucleotide chain (D1: p 9 l 28-31).

The problem to be solved by claim 1 can thus be regarded as the provision of an alternative method for the differentiation of the introduced nucleotide in the growing oligonucleotide.

The technology for the distinction of the incorporated nucleotides used in D1 is more recent than the technology used in the present application. The use of different labels for each nucleotide is commonplace in the art and used in the standard sequencing techniques such as Sanger Sequencing. Hence, the skilled person who looks for an alternative method to that used in D1 would certainly consider the standard technology of differentiated labelling as claimed (see also D2: abstract). Thus, claim 1 does not seem to involve inventive activity. Since dependent **claims 2-13** rely on common technology, they do not seem to contain an inventive concept, either.

2.2 Although novel, **claim 19** does not seem to be inventive:

The claim is directed to an array of immobilized polymerase systems, wherein the immobilized polymerase systems are not novel (see point 1.1 above). The arrangement of the systems in an array appears to belong to common technology (see appl.: p 6 para 3). Furthermore, D3 describes the use of template arrays immobilized on a solid support (D3: p 8 l 33- p 9 l 3). **Claims 20-23**, which pertain to embodiments with specific spacing distances of the polymerases, do not appear to be inventive, accordingly.

Re Item VI:

Certain published documents (Rule 70.10)

Application No Patent No	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
D4: WO 00/36152	22. June 2000	13. December 1999	14. December 1998 11. January 1999

The disclosure of D4 embraces all the technical features of **claims 14-23** (D4: p 2 l 28- p 4 l 12; p 6 l 12-28; p 15 l 10-13; p 21 l 13-16; claims 15-24; 27-30) .

Re Item VII

The expression "incorporated herein by reference" in respect of prior art documents (e.g. page 13 para 4) leads to a doubt as to whether the requirement of the description being self-contained is satisfied (Guidelines II, 4.17).

Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the document D1 is not mentioned in the description, nor is this document identified therein.

Re Item VIII

Claim 14 does not satisfy Art 6 PCT for the following reasons:

- The technical nature of a "reaction center" is not clear which renders the subject-matter for which protection is sought unclear.
- The claim is directed to "an immobilized polymerase system for contacting nucleic acids" and it encompasses (b) a nucleic acid sample. However, the technical nature of a "sample" is by definition not known. Hence, the subject-matter of claim 14 is not defined and thus unclear. Moreover, the "immobilized polymerase system" comprises a primer (c), but it is not clear from the claim whether the primer is immobilized or not. These two arguments also apply to **claim 19**, which is directed to an array of immobilized polymerase systems of claim 14.

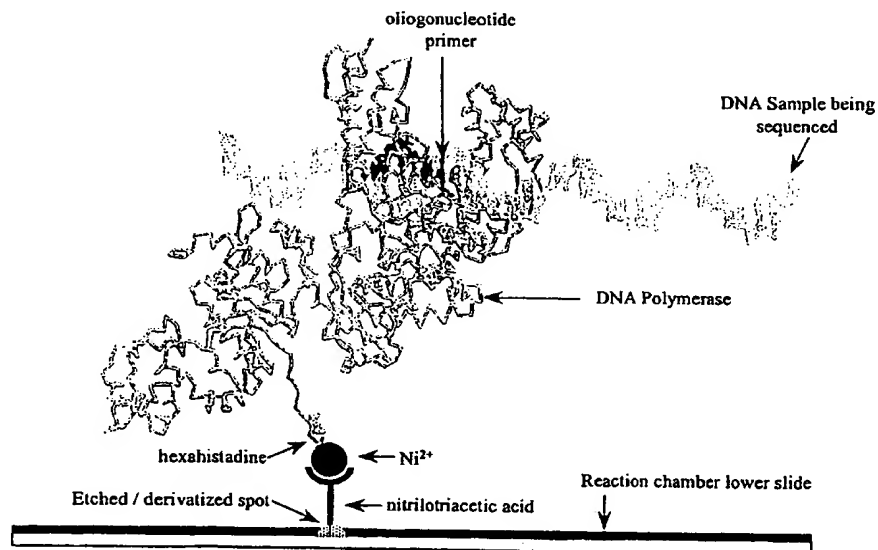
Claim 18 does not comply with Art 6 PCT because the term "modified T7 polymerase" is vague which renders the scope of the claim unclear.



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁷ : C12Q 1/68		A1	(11) International Publication Number: WO 00/53805
			(43) International Publication Date: 14 September 2000 (14.09.00)
(21) International Application Number: PCT/GB00/00873 (22) International Filing Date: 10 March 2000 (10.03.00) (30) Priority Data: 09/266,187 10 March 1999 (10.03.99) US (71) Applicant (for all designated States except US): ASM SCIENTIFIC, INC. [US/US]; 240 Norfolk Street, Cambridge, MA 02139 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): STEMPLE, Derek, Lyle [US/GB]; 292 Hatfield Road, St. Albans, Hertfordshire AL1 4UN (GB). ARMES, Niall, Antony [GB/GB]; 140 Long Lane, London N3 2HX (GB). (74) Agents: SCHLICH, George, William et al.; Mathys & Squire, 100 Gray's Inn Road, London WC1X 8AL (GB).		(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.	

(54) Title: A METHOD FOR DIRECT NUCLEIC ACID SEQUENCING



Example of a DNAS Reaction Center

(57) Abstract

The present invention provides a novel sequencing apparatus and the methods employed to determine the nucleotide sequence of many single nucleic acid molecules simultaneously, in parallel. The methods and apparatus of the present invention offer a rapid, cost effective, high through-put method by which nucleic acid molecules from any source can be readily sequenced without the need for prior amplification of the sample or prior knowledge of any sequence information.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
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EE	Estonia						

INTERNATIONAL SEARCH REPORT

Inter. Patent Application No

PCT/GB 00/00873

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- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

18 August 2000

Date of mailing of the international search report

28/08/2000

Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 00/00873

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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E	WO 00 36152 A (WILLIAMS JOHN G K ;LI COR INC (US)) 22 June 2000 (2000-06-22) the whole document -----	1-23

INTERNATIONAL SEARCH REPORT

information on patent family members

International Application No

PCT/GB 00/00873

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 9905315	A	04-02-1999	AU 8455998 A		16-02-1999
			EP 1017848 A		12-07-2000
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			JP 4505251 T		17-09-1992
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			AU 4020893 A		18-11-1993
			CA 2133956 A		28-10-1993
			DE 69314951 D		04-12-1997
			DE 69314951 T		19-03-1998
			EP 0640146 A		01-03-1995
			ES 2110604 T		16-02-1998
			JP 7507681 T		31-08-1995
			US 6087095 A		11-07-2000
GB 2102005	A	26-01-1983	NONE		
WO 9833939	A	06-08-1998	NONE		
WO 9106678	A	16-05-1991	CA 2044616 A		27-04-1991
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WO 9421822	A	29-09-1994	AU 687801 B		05-03-1998
			AU 6411694 A		11-10-1994
			CA 2158642 A		29-09-1994
			EP 0689610 A		03-01-1996
			JP 8507926 T		27-08-1996
			US 5622824 A		22-04-1997
			US 5872003 A		16-02-1999
			US 5851765 A		22-12-1998
			US 6074823 A		13-06-2000
WO 0036152	A	22-06-2000	WO 0036151 A		22-06-2000

INTERNATIONAL SEARCH REPORT

Inter. Application No

PCT/GB 00/00873

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, MEDLINE, BIOSIS, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 05315 A (DENSHAM DANIEL HENRY ;MEDICAL BIOSYSTEMS LTD (GB)) 4 February 1999 (1999-02-04) the whole document	1-23
A	WO 96 31622 A (ISIS INNOVATION ;SOUTHERN EDWIN MELLOR (GB); PRITCHARD CLARE ELIZA) 10 October 1996 (1996-10-10) the whole document	
A	WO 90 13666 A (AMERSHAM INT PLC) 15 November 1990 (1990-11-15) the whole document	
A	WO 93 21340 A (MEDICAL RES COUNCIL ;BRENNER SYDNEY (GB); ROSENTHAL ANDRE (GB)) 28 October 1993 (1993-10-28) the whole document	
	-/-	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
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- *8* document member of the same patent family

Date of the actual completion of the international search

18 August 2000

Date of mailing of the international search report

28/08/2000

Name and mailing address of the ISA

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Hagenmaier, S

INTERNATIONAL SEARCH REPORT

information on patent family members

International Application No

PCT/GB 00/00873

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INTERNATIONAL COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

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Date of mailing (day/month/year) 17 October 2000 (17.10.00)	
International application No. PCT/GB00/00873	Applicant's or agent's file reference GWS/MM/22204
International filing date (day/month/year) 10 March 2000 (10.03.00)	Priority date (day/month/year) 10 March 1999 (10.03.99)
Applicant STEMPLE, Derek, Lyle et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

22 September 2000 (22.09.00)

☐ in a notice effecting later election filed with the International Bureau on:
2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

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